

IN THE CLAIMS:

Claims 1-3 have been canceled.

Please cancel claims 8 and 27 without prejudice.

Please add new claim 37.

Claims 4-7, 9-17, 19-21, 24, 26, 28-29, and 31-36 have been amended.

Claims 1-3 (canceled).

4. (currently amended) A bioreactor apparatus and cell culturing system providing means for cell sampling, dilution, and fixation, comprising:

a sealed housing enclosing a cell growth reactor vessel;

a cell growth reactor vessel rotatable about its axis including a cylindrical side wall connecting ~~an upper~~ first reactor cover plate and a ~~lower~~ second reactor cover plate, ~~an upper a first~~ fluid rotary union providing an inlet for fluid communication with a fluid medium source, a ~~lower~~ second fluid rotary union including at least one exit outlet for medium and cells and at least one exit outlet is in fluid communication with a filter for retaining cells and passage of medium;

~~an electrical power source;~~

means for rotating said reactor vessel about its axis;

~~means for rotating one of said upper collector plate or said lower collector plate;~~

means for collecting fluid and cell samples comprising a rotary sample collector including a first stationary collector plate and a second rotatable collector plate in sealed connection at their centers and in fluid communication with said reactor vessel;

means for delivering medium and circulating medium to and from said reactor vessel;

~~a sealed compartment for sample collection bags providing a level of chemical containment for safety;~~

means for controlling the humidity within said sealed housing ~~reactor vessel;~~ and;

~~a rotary sample collector in fluid communication with said reactor vessel;~~

means for rotating one of said upper collector plate or said lower collector plate;

a computer ~~program~~ with graphical user interface for automatically and/or robotically controlling rotation of the reactor vessel, rotation of said first upper plate with respect to said second lower plate, controlling the feeding of fresh medium, controlling perfusing the reactor vessel, controlling taking timed collection samples of fluid from said reactor vessel, and selecting between collecting cells or cell-free supernatant; and

an electrical power source in electrical communication with said means for rotating said reactor vessel, said means for rotating said collector plate, and said means for delivering and circulating medium.

5. (Currently amended) The bioreactor apparatus and cell culturing system of claim 4, said rotary sample collector comprising multiple sample collectors in said second rotatable collector plate including an inlet rotatably alignable with an outlet in said first stationary collector plate with capability for collecting cells on filters, fixing the cells and collecting the cells.

6. (Currently amended) The bioreactor apparatus and cell culturing system of claim 4 said rotary sample collector including a rotating inlet into a compartment with a filter, means to remove waste liquid from an input cell suspension, means for collecting cells in chambers in liquid suspension, and means to store fixed cells for later recovery and examination. ~~the capability for collecting cells on filters, fixing the cells and collecting the cells.~~

~~7.(currently amended) The bioreactor apparatus and cell culturing system of claim 5;~~
A bioreactor apparatus and cell culturing system providing means for cell sampling, dilution, and fixation, comprising:

a sealed housing enclosing a cell growth reactor vessel;

a cell growth reactor vessel rotatable about its axis including a cylindrical side wall connecting a first reactor cover plate and a second reactor cover plate, a first fluid rotary union providing an inlet for fluid communication with a fluid medium source, a second fluid rotary union including at least one exit outlet for medium and cells and at least one exit outlet is in fluid communication with a filter for retaining cells and passage of medium;

means for rotating said reactor vessel about its axis;

means for collecting fluid and cell samples comprising a rotary sample collector including a first stationary collector plate and a second rotatable collector plate in sealed connection at their centers and in fluid communication with said reactor vessel;

means for delivering medium and circulating medium to and from said reactor vessel;

means for controlling the humidity within said sealed housing

means for rotating one of said upper collector plate or said lower collector plate;

a computer with graphical user interface for automatically and/or robotically controlling rotation of the reactor vessel, rotation of said first plate with respect to said second plate, controlling the feeding of fresh medium, controlling perfusing the reactor vessel, controlling taking timed collection samples of fluid from said reactor vessel, and selecting between collecting cells or cell-free supernatant;

an electrical power source in electrical communication with said means for rotating said reactor vessel, said means for rotating said collector plate, and said means for delivering and circulating medium; and

said rotary sample collector including multiple sample collectors having the capability for collecting cells on filters, fixing the cells and collecting the cells.

8.(canceled)

9.(currently amended) The bioreactor apparatus and cell culturing system of claim [[3]] 4, further comprising ~~wherein said~~ means for exchanging gases between the culture medium and ambient gases comprises a user selected length of permeable tubing and a peristaltic pump.

10.(currently amended) The bioreactor apparatus and cell culturing system of claim [[3]] 4, wherein said filter in said exit outlet of said second fluid rotary union ~~further comprising~~ comprises a low pressure drop filter for preventing cells from exiting the reactor when fluid is withdrawn. ~~through a selected one of the at least two outlets in the lower rotary union.~~

11.(currently amended) The bioreactor apparatus and cell culturing system of claim [[3]] 4 further comprising a polymeric fresh-medium storage bag in fluid communication with ~~said a~~ peristaltic pump for batch feeding, perfusion or sample collection connecting to said reactor vessel through a conduit.

12.(currently amended) ~~The bioreactor apparatus and cell culturing system of claim 3~~
A bioreactor apparatus and cell culturing system providing means for cell sampling, dilution, and fixation, comprising:
a sealed housing enclosing a cell growth reactor vessel;
a cell growth reactor vessel rotatable about its axis including a cylindrical side wall connecting a first reactor cover plate and a second reactor cover plate, a first fluid rotary union providing an inlet for fluid communication with a fluid medium source, a second fluid rotary union including at least one exit outlet for medium and cells and at least one exit outlet is in fluid communication with a filter for retaining cells and passage of medium;
means for rotating said reactor vessel about its axis;
means for delivering medium and circulating medium to and from said reactor vessel;
means for controlling the humidity within said sealed housing
a computer with graphical user interface for automatically and/or robotically controlling rotation of the reactor vessel, rotation of said first plate with respect to said second plate, controlling the feeding of fresh medium, controlling perfusing the reactor vessel, controlling taking timed collection samples of fluid from said reactor vessel, and selecting between collecting cells or cell-free supernatant;
an electrical power source in electrical communication with said means for rotating said reactor vessel and said means for delivering and circulating medium; and
means for collecting fluid and cell samples further comprising a manifold and a series of pinch valves in fluid communication with said sealed compartment for sample collection bags for the periodic collection of samples of suspended cells or cell-free medium.

13. (currently amended) The bioreactor apparatus and cell culturing system of claim[[3]] 4,

wherein said means for controlling the humidity comprises a humidity control system consisting of a polymeric porous matrix and a fan;

14. (currently amended) ~~The bioreactor apparatus and cell culturing system of claim 3~~

A bioreactor apparatus and cell culturing system providing means for cell sampling, dilution, and fixation, comprising:

a sealed housing enclosing a cell growth reactor vessel;

a cell growth reactor vessel rotatable about its axis including a cylindrical side wall connecting a first reactor cover plate and a second reactor cover plate, a first fluid rotary union providing an inlet for fluid communication with a fluid medium source, a second fluid rotary union including at least one exit outlet for medium and cells and at least one exit outlet is in fluid communication with a filter for retaining cells and passage of medium;

means for rotating said reactor vessel about its axis;

means for collecting fluid and cell samples comprising a rotary sample collector including a first stationary collector plate and a second rotatable collector plate in sealed connection at their centers and in fluid communication with said reactor vessel;

means for delivering medium and circulating medium to and from said reactor vessel;

means for controlling the humidity within said sealed housing

means for rotating one of said upper collector plate or said lower collector plate;

a computer with graphical user interface for automatically and/or robotically controlling rotation of the reactor vessel, rotation of said first plate with respect to said second plate, controlling the feeding of fresh medium, controlling perfusing the reactor vessel, controlling taking timed collection samples of fluid from said reactor vessel, and selecting between collecting cells or cell-free supernatant;

an electrical power source in electrical communication with said means for rotating said reactor vessel, said means for rotating said collector plate, and said means for delivering and circulating medium; and

wherein said rotary sample collector further comprises means for rotating inlet into a compartment with filter, means to remove waste liquid from an input cell suspension, means for

collecting cells in chambers in liquid suspension, and means to store fixed cells for later recovery and examination.

15.(currently amended) The bioreactor apparatus and cell culturing system of claim [[3]] 4, including means for oxygenation of medium in said reactor.

16.(currently amended) The bioreactor apparatus and cell culturing system of claim [[3]] 4, further including analytical sensors for measuring the pH, glucose, and oxygen of said medium.

17.(currently amended) The bioreactor apparatus and cell culturing system of claim [[3]], said means for rotating said second collector plate comprises a stepping motor for rotating and aligning said second rotatable collector plate with said first stationary collector plate.

18.(previously presented) The bioreactor apparatus and cell culturing system of claim 10, wherein said low pressure drop filter is a polymeric filter.

19.(currently amended) The bioreactor apparatus and cell culturing system of claim [[3]] 4, ~~further comprising a method [[fo]] of preventing cell capture on said drop filter.~~ said means for delivering medium and circulating medium to and from said reactor vessel comprises at least one perfusion pump.

20.(currently amended) The bioreactor apparatus and cell culturing system [[fo]] of claim [[3]] 4, further comprising ~~a video camera or video device and microscope system.~~ a camera and an observation system, comprising:

a video frame grabber;

a beam splitter for dual optical view of contents of said rotating cell growth reactor and of cell samples extracted from said cell growth reactor or a microscopic observation slide disposed in a fluid line from said reactor vessel;

at least one LED and a diffuser for providing backlighting for said microscopic observation

slide;

at least one LED providing front lighting or oblique lighting for viewing the contents of said cell growth reactor;

a camera attached to said housing containing a beamsplitter cube wherein a first side of said beamsplitter attaches to an objective lens for viewing said reactor contents and a second side of said beamsplitter attaches to a spacer barrel which is attached to said microscopic observation slide.

21.(Currently amended) The bioreactor apparatus and cell culturing system of claim 20, wherein said ~~video~~ camera system comprises a color camera and a dual optical path configuration allowing for a first observation of the rotating cell growth reactor contents with a 20 x 25mm Field Of View (FOV) and a second microscopic observation path providing an approximately 5-micron resolution of cell samples that have been extracted from the bioreactor and pumped into the observation cell.

22.(previously presented) The bioreactor apparatus of claim 21, wherein said digital camera and/or video device shows instantaneous or still frame pictures.

23.(canceled)

24.(currently amended) The bioreactor apparatus of claim ~~20~~ 3 ~~further comprising LEDs for providing uniform light to said reactor.~~ further comprising a turning prism in optical communication with said cell growth reactor and a foil type heater in radiant communication with said turning prism to prevent condensation.

25.(previously presented) The bioreactor apparatus of claim 23 further comprising LEDs for providing uniform light to said microscopic observation slide.

26.(currently amended) A bioreactor apparatus and cell culturing system, comprising:
~~a reactor vessel;~~

a cell growth reactor vessel rotatable about its axis including a cylindrical side wall connecting a first reactor cover plate and a second reactor cover plate, a first fluid rotary union providing an inlet for fluid communication with a fluid medium source, a second fluid rotary union including at least one exit outlet for medium and cells and at least one exit outlet is in fluid communication with a filter for retaining cells and passage of medium;

an electrical power source in electrical communication with said means for rotating said reactor vessel, said means for rotating said collector plate, and said means for delivering and circulating medium;

means for rotating said reactor vessel about its axis;

means for collecting fluid and cell samples comprising a rotary sample collector including a first stationary collector plate and a second rotatable collector plate in sealed connection at their centers and in fluid communication with said reactor vessel;

said rotary sample collector further comprises means for rotating inlet into a compartment with filter, means to remove waste liquid from an input cell suspension, means for collecting cells in chambers in liquid suspension, and means to store fixed cells for later recovery and examination.

means for delivering medium and circulating medium to and from said reactor vessel;

means for rotating one of said upper collector plate or said lower collector plate;

means of exchanging gases between said medium and ambient gas environments;

a computer program with graphical user interface for automatically and/or robotically controlling said reactor vessel;

a video camera or video device and microscope system wherein said video camera system comprises a camera and a dual optical path configuration allowing for an observation of said cell growth reactor contents and a second microscopic observation path a micron resolution of cell sample.

27.(cancelled)

28.(currently amended) The bioreactor and cell-culture system according to claim [[27]] 26, wherein said reactor vessel comprises at least one cylindrical wall and opposing end cover plates at

least one rotary unions sealed in fluid communication with end cover plates at least two external tubing connectors that articulate the reactor vessel with said closed loop.

29.(Currently amended) The bioreactor and cell-culture system according to claim 26 [[27]] wherein fluid movement within said closed loop is effected by at least one peristaltic, shuttle or similar pumps that act upon the tubing of the closed loop and do not contact the fluid directly.

30.(Previously presented) The bioreactor and cell-culture system according to claim 29 wherein said fluid movement is controlled by at least one electronically controlled pinch valves that acts upon the tubing of the closed loop and does not contact the fluid directly.

31.(Currently amended) The bioreactor and cell-culture system according to claim [[27]] 26 wherein said closed-loop bioreactor system is fully enclosed in a first sealed compartment proving a level of chemical containment for safety and in which containers used for sample collection are optionally enclosed within a second sealed container within said first sealed container for one additional level of chemical containment and therefore triple chemical containment for safety.

32.(Currently amended) The bioreactor and cell-culture system according to claim [[27]] 26 wherein said closed fluid loop includes a plurality of lines providing access for the addition of external fluid to said closed loop and the removal of waste and samples from said closed loop without violating two levels of chemical containment for safety, for making chemical measurements on line, for collecting and fixing cells automatically for immediate observation by an optionally include microscope, and for collection in sample containers.

33.(Currently amended) The bioreactor and cell-culture system according to claim [[27]] 26 further comprising means for measuring pH and dissolved oxygen content of said medium from said reactor vessel.

34.(Currently amended) The bioreactor and cell-culture system according to claim 26 [[27]]

further comprising a computer including programming for conducting sequences of experimental procedure requiring pumping , valving chemical measurement, reactor rotation rate, microscope operation without operator intervention or with optional operator intervention.

35.(Currently amended) The bioreactor and cell-culture system according to claim 26 [[27]] wherein said bioreactor and cell-culture system is capable fo functioning in low gravity and that fulfills safety requirements for manned space flight.

36.(Currently amended) The bioreactor and cell-culture system according to claim 26 [[27]] further comprising:

a microscope system for observing suspended cells or organisms within said bioreactor vessel, said microscope system comprising

an inlet from a branch of the closed loop coupled to a holder for a hollow microscope slide, a hollow microscope slide made of glass or fabricated by photo polymerization, a light-microscope objective compound lens, a video plane, an outlet for the removal of samples of fluid after observation, and reservoirs for the addition of reagents to cell suspensions when said reagents are required for observation.

Please add new claim 37 as follows:

–37. (New) The bioreactor and cell culture system of claim 4, further including means for oxygenation of medium in said cell growth reactor comprises passing filtered medium through thin-walled silicone tubing in an oxygen rich environment.--